The University of Chicago

DEUTERIUM EXCHANGE REACTIONS

A DISSERTATION SUBMITTED TO THE FACULTY OF THE DIVISION OF THE PHYSICAL SCIENCES IN CANDIDACY FOR THE DEGREE OF DOCTOR OF PHILOSOPHY

DEPARTMENT OF CHEMISTRY

1939

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ALEX H. WIDIGER

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I. PROOF OF THE STERIC NATURE OF THE ORTHO EFFECT IN AROMATIC TERTIARY AMINES[1]

It has previously been postulated[2] that the acid catalyzed hydrogen exchange reaction of dimethylaniline and its derivatives takes place through a direct addition of deuterons at the ortho or para positions giving rise to tautomeric forms of the amine salt. In view of the requirements in classical structural theory that the dialkylamino group should be coplanar with the quinonoid ring in these forms, it was possible to interpret the inhibiting effect of an ortho nitro group, which had been observed in a study of the exchange reactions of the nitrodimethylaniline, as a steric effect having to do with the obstruction offered by the nitro group to the attainment of a coplanar configuration. Several further examples of inhibition of the hydrogen exchange reactions have since been discovered and it is now obvious that the ortho effect is as characteristic for this reaction as it is for numerous other reactions of aromatic amines.[3]

In an effort to test experimentally the validity of this theory of the ortho effect in exchange reactions several independent lines of approach were explored. One line of attack was based on the argument that if the amino nitrogen were to be linked to the ortho carbon atom in such a way as to form a five membered ring which would necessarily be coplanar with the benzene ring, as in N-methyl indoline (I), there should be no ortho effect. A similar result could be predicted for an analogous compound with a six membered ring, N-methyltetrahydroquinoline (II), though perhaps with

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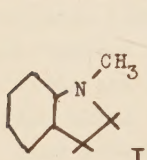
[1] Brown, Widiger, and Letang, J. Am. Chem. Soc (in press).

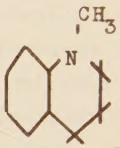
[2] Brown, Kharasch, and Sprowls, J. Org. Chem (in press).

[3] Friedlander, Monatsh., 19, 627 (1898); Gnehm and Blumer, Ann., 304, 87 (1898); Thomas., J. Chem. Soc., 103, 599 (1913); Karrer, Ber., 28, 1398 (1915); Braun, et al., Ber., 51, 282 (1918); Ley and Pfeiffer, Ber., 54, 363 (1921); Ley, et al., Ber., 58, 1765 (1925); Van Alphen, Rec. trav. chim., 46, 809 (1927); Huckel, Ber., 61, 1517 (1928); Anschutz, Z. Angew. Chem. 41, 691 (1928).

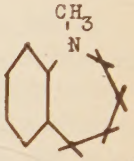
less certainty because of the probable slight strain involved in the planar configuration. With a highly puckered seven membered ring on the other hand, as in N-methyl -homo-tetrahydroquinoline (III), the opportunity for a steric effect of the type under consideration definitely arises and this compound should exhibit the characteristic inhibition of the normal lability of the para and unsubstituted ortho hydrogen atoms.



I



II



III

The experimental results are entirely in accordance with the predictions. In the series of cyclic bases it is observed that (I) and (II) exhibit a very high degree of reactivity in the exchange reaction, the former being more reactive but both exceeding dimethylaniline, whereas (III) exchanges its hydrogens at the very slow rate characteristic of an ortho effect compound. The results provide rather convincing evidence that the key to the situation really lies in the ability of the dialkylamino structure to come into the plane of the benzene ring.

Meanwhile one can approach the problem by evidence from another direction in studying the mechanism of exchange of the aromatic tertiary amines. It was held that if deuterons enter these free amines by direct attachment at a benzenoid carbon atom, the acid catalyst functioning as donor, and not by way of the normal amine salt (or cation), then on increasing the amount of acid the rate of exchange should reach a maximum value which would represent the most favorable compromise between the increasing concentration of acid catalyst and the decreasing concentration of free base. Experiments were carried out to determine the extent of the exchange reaction of dimethylaniline under an arbitrarily selected, but standardized, set of conditions with varying amounts of added acid. The results, which are shown in Figure 1, revealed that the rate of exchange beyond a certain point does indeed fail to keep pace with the increasing concentration of acid although a definite maximum does not appear in the range covered by the experiment.[1]

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[1]Experimental errors that could not be properly taken care of in our procedure, especially at high concentrations of acid,

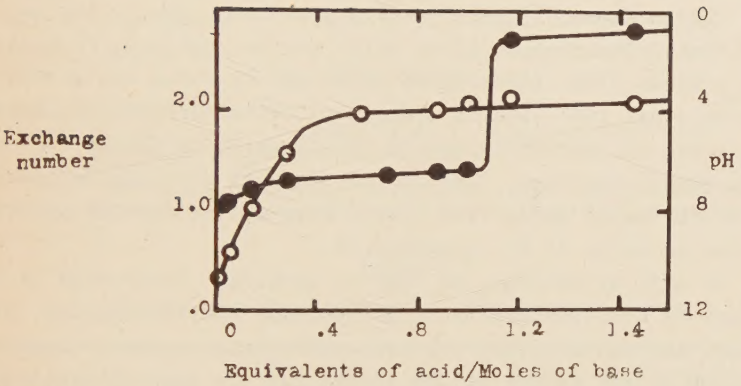

Fig. 1 The rate of exchange of dimethylaniline with varying amounts of acid.

○ Exchange rate
● pH

In order to determine the extent to which the ortho effect can be overcome by having present a suitably oriented activating group as an additional substituent, the behavior of a few substances fulfilling these requirements was investigated. The results show that the de-activating effect of an ortho methyl group which is evident in the failure of dimethyl o-toluidine and of 2-dimethyl amino m-xylidene to undergo exchange is alleviated to a small extent by a second methyl group meta to the dimethylamino group, as in dimethyl p-xylidene which exhibits a slow exchange reaction. The same phenomenon can be seen in the fact that 5-dimethylaminotetralin also exhibits a hydrogen exchange reaction although again it is a slow reaction. These results provide a clue to the behavior of α dimethylaminonaphthalene which can be regarded, formally at least, as an ortho substituted amine and in which there would seem to be cause for a steric effect but which nevertheless shows a high degree of reactivity and in this respect is almost comparable with dimethylaniline. We may then suppose that the activating effect of the benzo group very nearly compensates for the steric inhibition on which it is superimposed.

It will be obvious, in view of parallel occurrence of ortho effect in the hydrogen exchange reaction and in coupling, nitrosation, and condensation reaction of aromatic amines, that the elucidation of the nature of the effect for one type of reaction has important implications with regard to the others.

Experimental

The procedure for carrying out exchange reactions in deutero-alcohol is well described by Eberle[1] and so will not be repeated here. It has been improved to some extent, as will be noted in a later part of this dissertation, because of the discovery that deuteroalcohol is quite easily fractionated when distilled at re-

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limited the range of these experiments. It is nevertheless not certain that a decrease in the rate of exchange at still higher acid concentrations would be observed since exchange by a different, but closely related, mechanism would probably set in. This mechanism would be similar to that by which benzene exchanges hydrogen with sulfuric acid (Ingold, Wilson and Roisin, J. Chem. Soc., 1936, 915). These authors (ibid., 1639) obtained similar results for the exchange of dimethylaniline in aqueous hydrochloric acid.

[1] Eberle, Ph.D. dissertation, Department of Chemistry, The University of Chicago (1938).

TABLE 1[a]

EXCHANGE REACTIONS ON DIMETHYLANILINE DERIVATIVES

Compound	cc.100% H_2SO_4	Time Hrs.	Temp.	Initial D_2O	Final D_2O	Exchange Number
Dimethyl o-toluidine	.020	90	115	2.30	2.30	.00
Dimethyl o-toluidine	.080	70	115	2.25	2.26	.00
2-dimethylamino m-xylidene	.020	90	115	2.30	2.30	.00
2-dimethylamino m-xylidene	.080	90	115	2.25	2.26	.00
Dimethyl p-xylidene	.020	70	115	2.30	2.24	.20
5-dimethylamino tetralin	.020	74	115	2.29	2.24	.19
-dimethylnaphthylamine	.020	41	115	2.76	2.29	1.36

[a]The above reactions took place with .0130 moles of compound, .0850 moles of alcohol, and the designated amount of acid.

TABLE 2[a]

EXCHANGE REACTIONS OF N-ORTHO RING COMPOUNDS

Compound	Time Hrs.	Temp.	cc.100% H_2SO_4	Initial D_2O	Final D_2O	Exchange Number
N-methyl indolin ...	24	60.0	.010	2.80	2.25	1.58
N-methyl tetrahydroquinoline	24	60.0	.010	2.74	2.42	.87
N-methyl homo tetrahydroquinoline ...	44	60.0	.010	2.79	2.78	.00
N-methyl home tetramydroquinoline ...	70	120.0	.020	2.77	2.57	.85
Dimethylaniline	24	60.0	.010	2.81	2.75	.12

[a]The above reactions took place with .0130 moles of compound, .0850 moles of alcohol, and the designated amount of acid.

duced pressure. In order to avoid this error the distillations are now carried out at atmospheric pressure care being exercised in collecting the same fraction in each distillation, and with these precautions a constant decrease, amounting to 0.8 % of the concentration of deuterium, was obtained. Control experiments, in

TABLE 3[a]

EXCHANGE REACTIONS ON DIMETHYLANILINE WITH VARYING AMOUNTS OF ACID

cc.100% H_2SO_4	Equivalents acid / Moles of base	Initial D_2O	Final D_2O	Exchange Number	Estimated $(pH)_{alc}$
....	....	2.83	2.81	....	11.5
.005	.014	2.81	2.68	.32	8.2
.020	.058	2.78	2.56	.57	7.6
.050	.14	2.74	2.38	1.01	7.2
.100	.29	2.69	2.19	1.56	6.9
.200	.58	2.58	2.02	1.97	6.6
.300	.88	2.48	1.95	2.01	6.4
.342	1.00	2.44	1.91	2.10	6.3
.400	1.17	2.39	1.87	2.15	1.1
.500	1.46	2.29	1.81	2.09	.9

[a]The above exchange reactions took place with .0130 moles of dimethylaniline, .085 moles of alcohol, and the designated amount of acid at 60.0° for 69 hours. The pH values were estimated by calculating the hydrogen ion concentration from the ionization constant of dimethylaniline in water as $2 \cdot 10^{-10}$ and of ethyl alcohol as 10^{-16}.

which no catalyst was present, were carried out with each compound and in no case did we find evidence of exchange in the absence of added acid.

The experimental results are given in Tables 1, 2, 3 in which the extent of hydrogen exchange is expressed in terms of the "exchange number" which is used here as a matter of convenience and which is, by definition,[1] equal to $(a/s)\ (D_1-D_2/D_2)$ where a/s is the molar ration of alcohol to compound, and D_1 and D_2 are the initial and final concentrations of deuterium in the alcohol. Corrections were applied for the dilution of the deuterium by the normal hydrogen of the added sulfuric acid. In the experiments recorded in Table 3 the corrections become quite large with the higher concentrations of acid and there is some uncertainty as to how it should be applied. The analytical data in all cases refers to the mol per cent deuterium found in the water obtained by combustion of the alcohol.

[1]Brown, Kharasch, and Sprowls, op. cit.

Preparations

n-Dimethylaniline.--b.p. 188°/750 mm, n_D^{20} 1.5582.

n-Dimethyl o-toluidine.--Prepared by the methylation of o-toluidine hydrobromide with methyl alcohol at 150°.[1] Purified by the acetic anhydride method. b.p. 180°/750 mm, n_D^{20} 1.5255.

2-Dimethylamino m-xylene.--2 amino m-xylene (Eastman) was methylated with methyl iodide and sodium carbonate solution. Purified by the acetic anhydride method. b.p. 193-194°/748 mm, n_D^{20} 1.5138.

Dimethyl p-xylidene.--p-Xylidene (Eastman) was methylated in the usual manner with methyl sulphate and sodium carbonate solution. Purified by the acetic anhydride method. b.p. 199°/745 mm, n_D^{20} 1.5223.

5-Dimethylaminotetralin.--α-naphthylamine was reduced with sodium in boiling iso-amyl alcohol to 5-amino tetralin.[2] b.p. 149-152°/15 mm, n_D^{20} 1.6044. This was methylated with methyl sulphate to 5-dimethyl amino tetralin. b.p. 134-34.5°/16 mm, n_D^{20} 1.6224.

N-methyl indoline.--This compound was obtained by the following method after several unsuccessful attempts by other methods. Indol (Eastman's) was dissolved in dry dioxane and refluxed several hours with excess potassium in an atmosphere of nitrogen. The solution was allowed to cool, the excess potassium removed and 10 per cent excess methyl iodide was added based amount of potassium consumed. The mixture was warmed for one hour and then most of the dioxan removed under reduced pressure. The compound is steam distilled and purified in the usual manner.[3] b.p. 123-124°/20 mm, n_D^{20} 1.6060, yield 90 %. The N-methyl indol was reduced with zinc dust and hydrochloric acid to N-methyl indolin according to the method of Wenzing.[4] b.p. 102°/20 mm, n_D^{20} 1.5682, d_4^{20} 1.004, yield 35 %.

N-methyl tetrahydroquinoline.--Quinoline methiodide was reduced to N-methyl tetrahydroquinoline with the aid of granulated

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[1] Reinhardt and Staedel, Ber., 16, 29 (1883).

[2] Bamberger and Althausse, Ber., 21, 1786 (1888).

[3] Koizumi, Komoki, and Titani, Bull. Chem. Soc. Japan., 13 645 (1938).

[4] Wenzing, Ann., 239, 246 (1887).

zinc and hydrochloric acid according to the method of Feer and Koenigs.[1] b.p. 105-106°/8 mm, n_D^{20} 1.5843, d_4^{20} 1.030. The compound gradually becomes colored a bright red when exposed to air and the rate of coloration is enormously accelerated by the presence of traces of acid. Our exchange reactions were run with samples which were distilled into the reaction tube under high vacuum without subsequent exposure to air. Under these conditions no color was observed in the uncatalyzed reactions and a slight yellow occurred in the acid catalyzed exchange reactions.

N-methyl homo tetrahydroquinoline.--This compound had previously been prepared by Braun and Seeman[2] by a very long and tedious procedure in which the overall yield was very small. A careful examination of the problem led to the discovery that o-amino phenyl butyric acid, one of the later intermediates prepared by Braun in the long series of reactions which led to the synthesis of this seven membered ring compound, could be prepared very conveniently by the Beckman rearrangement of the p-toluene sulfonic ester of α-tetralone oxime.[3]

Since the overall yield for the entire synthesis is small it was necessary to find a very convenient method for making α-tetralone in large quantities at a reasonable cost. After investigating the preparation of α-tetralone by the air oxidation of tetralin, the following method was finally adopted. Air is gently bubbled through a suspension of finely powdered copper oxide in tetralin maintained at 90° for 100 hours. The product is fractionated under vacuum yielding 75 % of recovered tetralin and 20 % of a mixture of tetralol-tetralone. No appreciable separation of the tetralone from the tetralol was obtained by distillation methods, and the conversion of the tetralone into the oxime is not a feasible method as the oxime crystallizes slowly and incompletely from the solution. The tetralone-tetralol solution which contains about 75 % tetralone is oxidized completely to tetralone by excess chromic acid in glacial acetic acid solution being careful to keep the solution cooled below 20°. The oxime is prepared from sodium acetate and technical hydroxylamine sulphate. The oxime is recrystal-

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[1] Feer and Koenigs, Ber., 18, 2388 (1885).

[2] Braun and Seeman, Ber., 55, 3824 (1922).

[3] Schroeter, Ber., 63, 1323 (1930).

lized from 50 % alcohol using a little Norite, m.p. 102°, yield 90 %. The oxime is converted into the ester of p-toluene sulfonic acid by the method suggested by Schroeter.[1] A mechanically stirred solution of 100 g. of the oxime and 140 g. of p-toluene sulfonyl chloride in one liter of acetone is slowly treated with 45 g. of flake potassium hydroxide in several portions over a period of several hours at 50°. Yield 70-85 %. The ester is rearranged in methyl alcohol at 100° to the p-toluene sulfonic acid salt of o-amino γ phenyl methyl butyrate. The most satisfactory apparatus is a two inch diameter, two foot long pipe fitted with caps and lined with a two inch pyrex tube sealed only at one end. The method is well described by Schroeter.[2] The ester is liberated with sodium acetate, extracted with ether, dried, and distilled in vacuum, b.p. 134°/1 mm. The ester slowly decomposes to the lactam during the distillation. The lactam reacts as readily as the ester in the next step so that as much volatile material as would come over was collected in the above distillation. The last fraction distilled with difficulty at 140° and solidified when cooled. Yield 65 %. The method of v Braun and Bartsch[3] was used to convert the above compound to homo tetrahydroquinoline. The ester or lactam in 10 g. batches was reduced with sodium in specially dried absolute alcohol to o-amino γ phenyl n-butyl alcohol. This was converted into o-amino γ phenyl n-butyl chloride by treatment with concentrated hydrochloric acid. The compound was cyclicized by steam distilling from an alkaline solution. The product obtained from 25 reductions was distilled in vacuum and yielded 30 g. of the amine: b.p. 114-116°/10 mm. n_D^{20} 1.5751, d_4^{20} 1.032. The amine was methylated with methyl iodide by refluxing equal volumes of the amine and methyl iodide with an equal volume of methyl alcohol at 65° for 3 hours. The product was purified by the acetic anhydride method: b.p. 105-106°/10 mm, n_D^{20} 1.5597, d_4^{20} 1.001, yield 65 %.

II. A STUDY OF ACID CATALYZED POLYMERIZATIONS

The polymerization of olefins may take place under the catalytic influence of a wide variety of substances. The polymerized olefins have only been investigated for their physical properties

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[1] Ibid. [2] Ibid.

[3] Braun and Bartsch, Ber., 45, 3376 (1912).

in relation to their industrial value and very little attempt has been made to determine their molecular structure. In a few cases the structure of some of the dimers and trimers obtained in these polymerizations has been determined and these results have been of immense value in determining a possible mechanism by which these polymerizations may take place. The study of polymerizations is a difficult problem because the investigator is confronted with many obstacles among which may be mentioned the lack of accurate analytical procedure for the analysis of the isomeric polymers produced in polymerizations, the attendent complications in the polymerizations because of isomerization and rearrangement of olefins, and the everpresent possibility that the reaction may be influenced by catalysts other than the one considered.

In this article we will confine ourselves to an investigation of the mechanism of acid catalyzed polymerizations of olefins with the aid of isotope exchange reactions. A large number of mechanisms for the acid catalyzed polymerizations of olefins have been postulated but they all have received criticism because of the lack of supporting evidence or their inability to explain all the isomers produced. These mechanisms will now be briefly mentioned with special emphasis placed on those mechanisms which involve proton transferrence.

After an exhaustive study of the polymerization of isomeric amylenes in sulfuric acid, Norris and Joubert[1] suggested that the polymerization proceeds through the initial formation of an alcohol which proceeds to react with another alcohol molecule to form the dimer and water. They believe they have substantiated their mechanism by demonstrating that olefins which can form a tertiary alcohol polymerize in more dilute acid than those olefins which can form a secondary alcohol.

Whitmore's mechanism[2] has received general acceptance. His interpretation is that the action of acids on olefins takes place by the stepwise addition of a proton to an olefinic carbon atom leaving the other carbon atom with only six electrons in its outer valence shell. This positive carbonium ion may undergo one of a series of reactions which are illustrated in Figure 2. Carbonium

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[1] Norris and Joubert, J. Am. Chem. Soc., 49, 873 (1927).

[2] Whitmore, Ind. Eng. Chem., 26, 94 (1934).

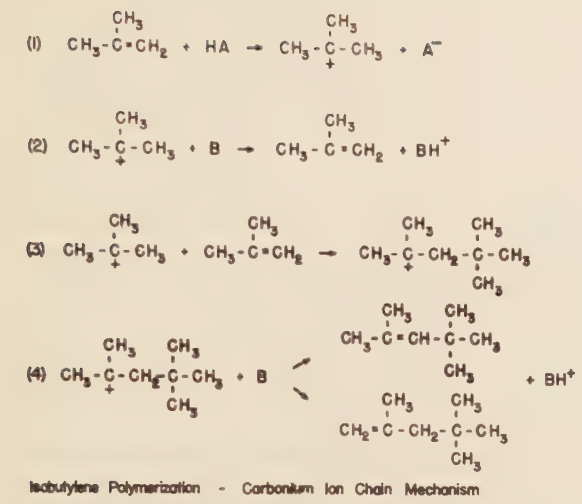

(1) CH3-C(CH3)=CH2 + HA → CH3-C+(CH3)-CH3 + A−
(2) CH3-C+(CH3)-CH3 + B → CH3-C(CH3)=CH2 + BH+
(3) CH3-C+(CH3)-CH3 + CH3-C(CH3)=CH2 → CH3-C+(CH3)-CH2-C(CH3)2-CH3
(4) CH3-C+(CH3)-CH2-C(CH3)2-CH3 + B → CH3-C(CH3)=CH-C(CH3)2-CH3 + BH+
CH2=C(CH3)-CH2-C(CH3)2-CH3
Isobutylene Polymerization - Carbonium Ion Chain Mechanism

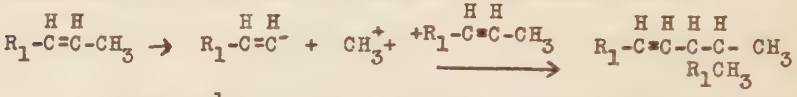
Fig. 2.

ions may undergo the reverse reaction of formation and revert to an olefin which need not possess its original structure as isomerization can easily take place by loss of a proton from any carbon atom adjacent to the six electron carbon atoms. Since the positive carbonium ion possesses a six electron carbon atom, the molecule may undergo a rearrangement (Wagner-Meerwein rearrangement) by migration of an alkyl radical yielding an isomeric compound. Whitmore claims these rearrangements are not of uncommon occurrence in polymerization of olefins. The positive carbonium ion may add an anion and thus form a saturated molecule as for example an alkyl halide. Or finally, the positive carbonium ion may add as such to an olefin to yield another positive carbonium ion which is of higher molecular weight. This molecule may then undergo any one or all of the above reactions and ad infinitim.

Because a certain dimer obtained in the polymerization of a pentene could not be accounted for by Whitmore's mechanism if one considers rearrangements to be improbable, Drake[1] has presented a novel mechanism for the polymerization of olefins. Drake postulates the transitory existence of positive and negative (in refer-

[1]Drake, J. Am. Chem. Soc., 56, 2076 (1934); Kline and Drake, J. Research, Nat. Bur. of Standards., 13, 705 (1934).

ence to Kharasch's scale of electronegativity) radicals which are formed by cleavage of the C-C bond adjacent to the olefin bond, and that these radicals are immediately adsorbed into other olefin molecules yielding the polymers as illustrated below.



Ipatieff[1] assumes that polymerizations of olefins which are catalysed by phosphoric acid proceed through the intermediate formation of phosphoric esters.

Dostel and Mark[2] using kinetic studies to support their mechanism suggest that all olefin polymerizations are caused by "activated molecules" which combine with another "activated molecule" or with a normal olefin molecule to form the polymers. The catalyst is responsible for the formation of these activated molecules.

All olefin polymerizations except the rarely occurring cyclizations such as occur in the butadiene compounds involve proton (or hydrogen atom) transferrence reactions as an intermediate step in the polymerization reaction. If deuterons are available in the solvent it is then possible to determine if proton transferrence reactions occur by the analysis of the products of the reaction for deuterium content. Some of these polymerizations in deuterosolvents have been investigated and the results are discussed below.

According to Whitmore's mechanism if we conduct the polymerization in deutero solvents we should expect the dimer to contain one more unit atom of proton-deuteron exchange per molecule of dimer than that of the monomer. The addition of anions to the positive carbonium ion and the isomerization of positive carbonium ions by proton transfer will both cause exchange without polymerization in competition with the exchange which can take place if Whitmore's mechanism is valid. It is thus apparent that kinetic studies of the polymerization process in deuterosolvents are necessary for a complete understanding of the reaction. One must not overlook the fact that the polymers themselves may exchange at a

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[1] Ipatieff, Paper presented before the New York meeting of the American Chemical Society, April (1935).

[2] Dostel and Mark, Trans. Faraday Soc., 32; 54 (1936).

variable rate which introduces another exchange reaction to further complicate the problem. Anethole, p-methoxy βmethyl styrene, is an ideal example of an acid catalyzed polymerization that yields only a dimer which because of its structure is incapable of further exchange. The polymerization of anethole under the influence of various catalysts to yield different compounds presents an interesting example of the specific effect of catalysts which is undoubtedly similar to the specific effect of catalyst observed in a more thorough investigation of the polymerization of 1,1-diphenylethylene which is illustrated in Figure 3.[1] There seems to be no doubt that the polymerization of anethole under the influence of the different types of catalyst produces analogous compounds although only one compound, isoanethole, has been isolated and its structure determined. Staudinger[2] has done considerable work on the polymers of anethole. The polymerization of anethole to isoanethole and the other types of polymerizations with their hypothetical products are given in Figure 4. The polymerization of anethole to isoanethole in deuterosolvents as predicted by Whitmore's mechanism is given in its entirety in Figure 5.

The polymerization is conducted according to the procedure of Goodal and Haworth[3] in 5N hydrochloric acid methyl alcohol solution. The results indicate that the reaction definitely does not take place through a proton addition reaction as has been postulated by Whitmore. The data, summarized in Figure 6, demonstrate that exchange occurs but that it is due to the rapid addition and loss of hydrogen chloride to the aliphatic double bond and not by the mechanism of polymerization which was illustrated. We have investigated the action of peroxides such as benzoyl peroxide and antioxidants such as isoamyl nitrite on the rate of polymerization as compared with the normal polymerization reaction. Although the results indicate that Whitmore's mechanism is not valid for this case, they nevertheless do not invalidate his mechanism as styrene polymerizations are known to take place with unusual ease. Anethole does not exchange or polymerize when refluxed with deuteroacetic acid which indicates that the acid strength of the solution

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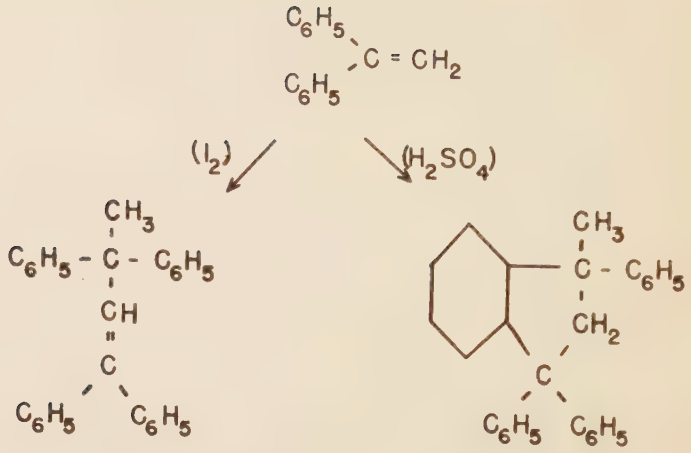
[1] Bergman and Weisz, Ann., 480, 49 (1930).

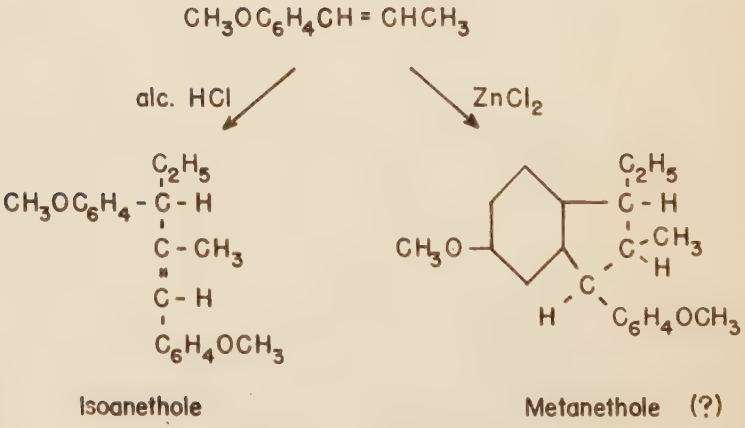
[2] Staudinger and Dreher, Ann., 517, 73 (1935).

[3] Goodall and Haworth, J. Chem. Soc., 2484 (1930).



Polymerization of as-diphenylethylene

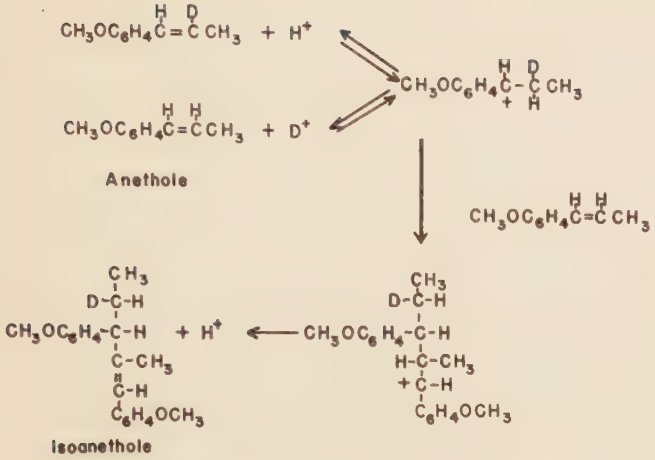
Fig. 3.



Isoanethole Metanethole (?)

Polymerization of Anethole

Fig. 4.



Polymerization of Anethole in Deutero-alcoholic-HCl

Fig. 5.

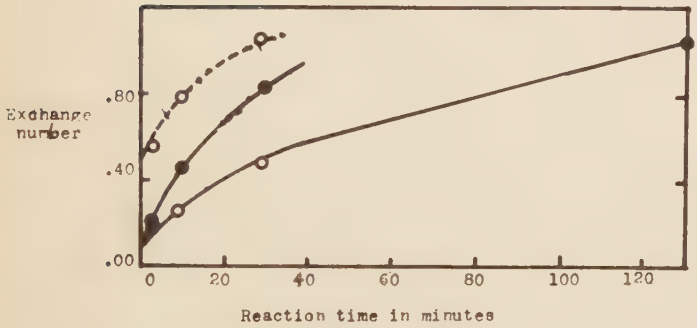


Fig. 6.--The exchange reactions of anethole during its polymerization.

O isoanethole (observed)
● anethole (observed)
-- isoanethole (calculated on the assumption that the reaction proceeds through the mechanism postulated by Whitmore)

is a significant factor in the polymerization.

The position of the deuterium in the dimer, isoanethole, was easily demonstrated. Isoanethole which had an exchange number of .46 was oxidized with alkaline permanganate and acetone to anisic acid and the ketone, 3 p-anisyl, 2 pentanone, according to the method described by Goodall and Haworth.[1] The anisic acid contained no deuterium indicating that no nuclear exchange had taken place. The ketone contained 95 % of the deuterium originally present in the isoanethole molecule.

The exchange reactions of the dienes were also investigated. The dienes were expected to exchange with ease because of their ability to undergo coupling reactions with diazonium salts[2] which indicates proton lability. We have found that the dienes exchange very slowly in the absence of polymerization but they exchange when conditions are such that polymerization also occurs. Solvent effects were found to be very important in that no exchange or polymerization occurred in alcohol while they do occur in acetic acid under the same conditions. 2,3-Dimethylbutadiene was found to exchange with greater ease than butadiene. The high molecular weight polymers were found to contain more deuterium than the dimers which may indicate a chain reaction but it may also be due to the possible greater ease of exchange of the dimers without further polymerization in comparison to exchange ease of the polymer. A significant factor not to be overlooked is that under the conditions by which the polymerizations take place, the chief dimer produced is a vinylcyclohexene derivative[3] whose formation may be due to a Diels-Alder type of reaction which does not necessitate proton transferrence.

Cyclohexene polymerizes slowly in alcohol or acetic acid containing a small amount of sulfuric acid but the product contains no deuterium. According to the Whitmore mechanism slow polymerization such as the above should permit a large amount of exchange.

The above results are too few in number and are limited to isolated examples of specific types of acid catalyzed polymerizations so that we feel unjustified in drawing any conclusions from them. The work is being continued.

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[1] Ibid.

[2] Meyer, Ber., 52, 1469 (1918).

[3] Farmer, J. Chem. Soc., 12 (1938).

Experimental

The technique employed in analyses of compounds for deuterium is the same as that described in the previous part of this dissertation. In some cases the compound wasn't sufficiently volatile to permit it to be combusted by the wick method so that it had to be combusted in a combustion tube using the procedure described by Mighton.[1]

Anethole.--(Eastman): b.p. 225°/750 mm. The polymerization was conducted in the manner described in the literature.[2] Merck's reagent methyl alcohol was treated with heavy water to yield heavy methyl alcohol by the same procedure in which deuteroalcohol is prepared. The deuteromethanol was then treated with dry hydrogen chloride until a 5N solution was obtained. The deuterium content was determined by treating a definite amount of the solution with a 10 % excess of vacuum dried silver oxide. The liquid was removed by distillation in high vacuum and the solution analyzed in the usual manner. In the following table are given the results obtained from a kinetic study of the polymerization reaction. The solution was alternately cooled, the lower liquid layer removed, and the solution again heated until the operation was repeated. The precipitated liquid was washed with strong alkali, dried, and distilled in vacuum. At 1 mm. pressure the unreacted anethole distilled over below 100° and the residue consisted of the dimer, isoanethole. The compounds were combusted in an atmosphere rich in oxygen in a combustion tube and the deuterium content of the obtained water was determined by the float method.

2,3-Dimethylbutadiene.--This compound was prepared by the dehydration of anhydrous pinacol with the aid of a small amount of iodine: b.p. 69-70/750 mm.

The exchange reactions of this compound were thoroughly investigated. Since Meyer's work[3] on the coupling reactions of the dienes indicates the possibility of proton lability, we investigated the exchange reaction of the most reactive diene, 2,3-dimethylbutadiene under the same conditions which Meyer has used in his coupl-

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[1]Mighton, Ph.D. dissertation, Department of Chemistry, The University of Chicago (1938).

[2]Goodall and Haworth, op. cit.

[3]Meyer, op. cit.

TABLE 4

THE POLYMERIZATION OF ANETHOLE[a]

Fraction Number	Reflux Time Minutes	Weight of Fractions	Compound	%D_2O	Exchange Number Anethole Unit
1	3	15 g.	anethole	.155	.21
		7	isoanethole	.135	.18
2	6	7	anethole	.33	.45
		2	isoanethole	.18	.24
3	20	4	anethole	.61	.83
		7	isoanethole	.358	.48
4	120	4	isoanethole	.775	1.05

[a]The reaction took place between 355 cc. (331 g.) of 5.3N hydrochloric acid and methanol with 71 g. of anethole. The deuterium content of the solvent as determined from the combustion of the solution as previously described was 8.90 % ionizable deuterium. Since the mole ratio of anethole to that of the hydrogen ion in the solvent is very small the dilution effect of the exchange reaction was ignored, and the value for complete exchange reaction of anethole is 8.90/12=.74 % D_2O. The compounds contained chlorine but this was found to be of a small percentage by Parr bomb analysis.

Table 5

EXCHANGE REACTIONS OF 2,3 DIMETHYLBUTADIENE[a]

Solvent	Catalyst	Time Days	Initial D_2O	Initial D_2O	Exchange Number	Remarks
Ethanol	1%H_2SO_4	4	.00	.15	.08	Slight polymerization
Ethanol	1% Na	4	.00	.06	.03	Slight polymerization
Acetic Acid		4	.00	.00	.00	Colorless
Acetic Acid	1%H_2SO_4	7	.00	1.23	2.10	Much polymerization
Acetic Acid	1%NaAc	4	.00	.00	.00	Colorless
Acetic Acid	1%$ZnCl_2$	4	.00	.00	.00	Some polymerization
Acetic Acid	2%H_2O	4	.00	.00	.00	Colorless

[a]In the above table 5 cc. of deuterium containing solvent and 5 cc. of the compound were reacted for the designated time at room temperature. The compounds were analyzed for deuterium in the same manner as described in the previous section on the polymerization of anethole. The compounds which were extensively polymerized were analyzed in a combustion tube. The deuterium content of the ethanol was 17.82% C_2H_5OD and that of the acetic acid was 11.80% CH_3COOD. The CH_3COOD was made from acetic anhydride and 12 % D_2O.

ing reactions. The preceding data indicate that in most cases, exchange takes place under the same conditions as does coupling with concomitant polymerization.

1,3 Butadiene.--The compound was obtained from butadiene tetrabromide with the aid of zinc and alcohol as is described by Margolis.[1] The product was distilled into the tared reaction tube under high vacuum, the apparatus re-evacuuated, and the tube sealed off and weighed. In the following reactions the solvent was purified by distillation and analyzed by the usual method neglecting the small error due to contamination of the solvent by the dimer of butadiene. The initial deuterium concentrations are the same as that given in the previous section on the polymerization of 2,3 dimethylbutadiene. The amount of butadiene varied from 1 to 1.5 gl and is not stated here because no exchanges occurred.

The results indicate that butadiene exchanges at a very slow rate in the experiments which we have conducted.

TABLE 6

EXCHANGE REACTIONS OF BUTADIENE

Solvent	Catalyst	Time Days	Temp.	Initial D_2O	Final D_2O	Remarks
EtOH	None	4	25	2.97	2.97	No polymerization
EtOh	5% H_2SO_4	3	25	2.90	2.92	No polymerization
EtOH	1% H_2SO_4	4	77	2.95	2.97	Slight polymerization
Hac	None	3	25	2.97	2.95	No polymerization
Hac	1% H_2SO_4	1	25	2.94	2.95	Much polymerization

1,3 Dimethylbutadiene.--This compound was prepared according to the method of Kyriakides[2] from the glycol obtained by reducing diacetone alcohol with sodium amalgam. The compound did not exchange in alcohol in the presence of sodium ethylate, but did exchange to a slight extent (exchange number .04) in the presence of 1 % sulfuric acid.

Cyclohexene.--(Eastman), b.p. 81°750 mm. A 1 % solution of sulfuric acid in 5 cc. of deuteroalcohol and 5 cc. of cyclo-

[1]Margolis, Ph. D. dissertation, Department of Chemistry, The University of Chicago (1936).

[2]Kyriakides, J. Am. Chem. Soc., 36, 988 (1914).

hexene were permitted to react at room temperature for 7 days. Analysis for deuterium content revealed that only a very small exchange (exchange number .04) had occurred with a little polymerization. In another experiment with .040 cc. sulfuric acid, 5 cc. of cyclohexene, and 5 cc. of deuteroacetic acid only a very small amount of exchange occurred (exchange number .04) after reacting 5 days at room temperature with a considerable amount (about 25%) of polymerization.

Cyclohexene does not appreciably exchange when it polymerizes in deuterosolvents containing an acid catalyst.

III. FRACTIONATION OF THE HYDROGEN ISOTOPES IN THE DISTILLATION OF ETHYL ALCOHOL[1]

During the course of some experiments on hydrogen exchange reactions in deuteroalcohol in which it was necessary to recover the alcohol from the mixtures for deuterium analysis by careful fractional distillation under reduced pressure, using small laboratory columns, we had occasion to suspect that serious errors were being introduced as a result of fractionation of the hydrogen sisotopes during the distillations. In view of the small mass difference between C_2H_5OD and C_2H_5OH, and the difficulty of accomplishing the desired separations (e.g. phenylacetylene and alcohol) with our columns, the possibility of accounting for our results on this basis was not considered seriously until after a number of more obvious possible sources of error had been eliminated. It was nevertheless possible to show, by distillations of alcohol alone, that the degree of isotopic separation is fully capable of accounting for our previous results.

The first distillations were carried out with a vacuum jacketed column, 4mm. I. D., 45 cm. in length, containing a spiral Nichrome wire packing. In a typical experiment, a sample of alcohol containing 17.8 % C_2H_5OD was distilled at 40 mm. pressure, and the first half of distillate was found to contain 14.8 % C_2H_5OD. The boiler residue was correspondingly richer in deuterium and contained 21.1 % C_2H_5OD. In order to compare the separation with that to be obtained on the distillation of water, a sample of water containing 3.06%D_2O was distilled under similar conditions and the

[1] Widiger and Brown, J. Am. Chem. Soc. (in press).

distillate was found to contain 2.43 % D_2O. These results would indicate that the fractionation of the hydroxyl hydrogen in alcohol takes place with very nearly the same efficiency as the fractionation of the isotopic forms of water. However, some allowance would have to be made for the fact that this column could not be made to operate smoothly in distillations of water.

These results immediately suggested that the distillation of alcohol with the aid of high-efficiency fractionating columns might prove to be a practicable method for the concentration of deuterium in quantity. The concentration of deuterium by the distillation of water has not thus far been a conspicuous success and it appears to be common experience that the efficiency of fractionating columns in such distillations does not approach that predicted on the basis of performance with organic liquids. The method of distilling alcohol offers a number of advantages from the standpoint of column operation and it was therefore of interest, although there is no intention of pursuing the project further at this time, to determine the degree of isotope separation obtainable with a more efficient column than that described above.

Subsequent distillations were carried out using a column packed with single turn glass helices, packed length 2.2 m., internal diameter 18 mm. The theoretical plate equivalent of this column was estimated to be in the neighborhood of 25 plates, this estimate being based on its performance in the separation of active amyl and isoamyl alcohols.[1] The results of two distillations, one at atmospheric pressure (750 mm.), the other at 80 mm. pressure, of deuteroalcohol containing 6.0 % C_2H_5OD initially are shown in Figure 7. The isotopic separation obtained corresponds to a fractionation factor 1.6 for the distillation at atmospheric pressure, and a factor 2.4 for the distillation at 80 mm. pressure. Assuming a column efficiency of 25 plates, the enrichment factors for the vaporization process are as follows; at 750 mm. 1.019 and at 80 mm. pressure 1.035.

In a distillation at atmospheric pressure of water containing 0.330 % D_2O, the first fraction of the distillate was found to contain 0.195 % D_2O. Before this experiment was carried out the column was thoroughly cleaned by distilling nitric acid through it,

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[1]This work on the amyl alcohols was carried out by Mr. W. de Atley.

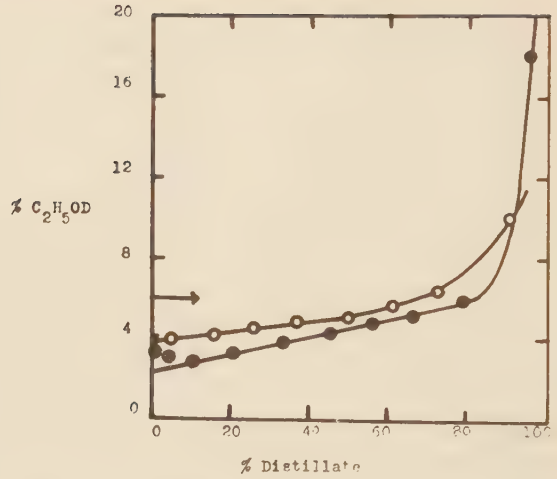

Fig. 7.--Fractional distillation of the hydrogen isotopes in ethyl alcohol containing an initial concentration of 6.00 % C_2H_5OD. O , atmospheric pressure; ● , 80 mm. pressure.

in order to facilitate uniform wetting of the packing, and no difficulty was experienced in the subsequent operation of the column with pure water. The observed fractionation factor, 1.69, is slightly higher than that found in the distillation of alcohol, and if we again assume a column efficiency of 25 plates we obtain an enrichment factor, 1.021. This is appreciably lower than the value, 1.025, reported by Urey and Teal[1] and our estimate of the column efficiency was therefore, for this distillation at least, too high.

The fact that a partial separation of the hydrogen isotopes can be readily effected by the distillation of water has been known for some time[2] and consequently the possibility of errors arising from this source in work on exchange reactions in heavy water has been recognized almost from the beginning. It is now evident that effects of this type can be equally significant in work on exchange reactions in heavy alcohol and that the necessary precautions will have to be taken to minimize the resulting errors.

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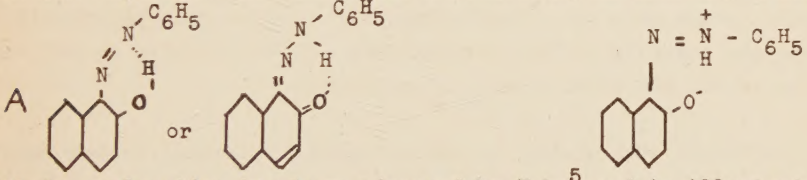
[1]Urey and Teal, Rev. Mod. Phys., 7, 48 (1935).

[2]Washburn and Smith, J. Chem. Phys., 1, 426 (1933); Lewis and Cornish, J. Am. Chem. Soc., 55, 2616 (1933); Hall and Jones, ibid., 56, 749 (1934).

IV. MISCELLANEOUS EXCHANGE REACTIONS

The Cannizzaro reaction of benzaldehyde in heavy water has been investigated by Bonhoeffer and Fredenhagen[1] who found that no exchange occurs in the reaction. We felt that this significant result should be checked and so we repeated the work in heavy water and in heavy alcohol and found that Bonhoeffer's results are essentially correct. We contemplated an investigation of the benzoin condensation but unfortunately the product of the condensation, benzoin, is not soluble in our solvent or mixed solvents which forced us to abandon the problem.

Benzeneazo-β-naphthol possesses the peculiar property of not forming a soluble sodium salt[2] in strong sodium hydroxide solution in contrast to benzeneazo-α-naphthol which does form a sodium salt.[3] Two explanations have been advanced to explain this property. A chelate ring, as in A, may reduce the ionization of the phenolic hydrogen and thus cause insolubility in alkali.[4] A more



likely explanation has been advanced by Kuhn[5] and is illustrated in diagram B. We have investigated the exchange reactions of this compound and found that the compound exchanges one hydrogen atom almost instantly at room temperature in deuteroalcohol and benzene in the absence of a catalyst. The result indicates that the compound is appreciably ionized but it does not exclude or favor any one of the above structures.

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[1]Bonhoeffer and Frenenhagen, Z. Physik. Chem., Abt. A., 181, 379 (1938).

[2]McPherson, Ber., 28, 2418 (1895).

[3]Lieberman, Ber., 16, 2858 (1883).

[4]Pheiffer and Mason, J. Soc. Dyers and Colour, 48, 293 (1932).

[5]Kuhn, Naturwiss., 20, 622 (1932).

V. SUMMARY

Some further examples of inhibition by ortho substitutents of the acid catalyzed hydrogen exchange reactions of dimethylaniline derivatives are reported.

The theory of the ortho effect is primarily a steric effect having to do with the tendency of the ortho substituent to block formation of quinonoid structures is supported by the results observed in the series of cyclic bases; N-methylindolin, N-methyltetrahydroquinoline, and N-methyl-homo-tetrahydroquinoline. The first two compounds in which the bicyclic structure is coplanar or nearly so showed no ortho effect while the third compound which has a highly puckered ring did show a characteristic ortho effect.

Acid catalyzed polymerizations of olefins were conducted in deuterosolvents to determine whether the mechanism of polymerization involves the addition and subsequent loss of a proton. The results in the case of anethole indicate that proton transferrence as the mechanism of polymerization does not occur while in the aliphatic series the results are inconclusive.

It has been shown, by distillation of alcohol in laboratory fractionating columns, that the isotopic forms of C_2H_5OH and C_2H_5OD may be partially separated, the degree of separation being comparable with that observed in the distillation of heavy water.